

REMARKS

Entry of the specification and amended and new claims is respectfully requested; no new matter is presented as the claims are supported by the specification. Amendments to the specification are offered in order to correct misspellings; entry is respectfully requested.

Claims 22, 23, 25-36 and 83-104 are pending in the instant application. Reconsideration and allowance of the claims are respectfully requested.

In paragraph 1 of the Office Action claims 22 and 84 were rejected under 35 U.S.C. § 112, first paragraph, "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Specifically, the Examiner explained that, regarding the percentage limitation of the effervescent couple "in an amount between about 5% and about 80%," "the instant application does not this range." It is noted that the last phrase of the previous sentence is incomplete, in that there is no specific statement regarding the failure of the instant specification with regard to the stated range. However, Applicants have assumed for the purposes of the rejection and this response that the Examiner intended to state, "the instant application does not explicitly recite this range." If Applicants have made an incorrect assumption, correction would be appreciated, as well as an opportunity to provide a response appropriate to the corrected statement.

Furthermore, the Examiner explained that the rejection of claim 22 is also with regard to the limitation that the couple is "greater than the amount necessary for tablet disintegration" because the specification doesn't "contain any

reference to what amount this may be or where this limitation may be found."

The rejections under 35 U.S.C. § 112, first paragraph, as explained above are traversed.

The Examiner has stated that the subject matter objected to "was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." However, although the standard is appropriately expressed, the Examiner has not satisfied "the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the specification disclosure a description of the invention defined by the claims." *Ex parte Sorenson*, 3 U.S.P.Q. 1462, 1463 (Bd. Pat. App. & Int'l 1987). In the interest of advancing prosecution, Applicant will take this opportunity to explain why there is evidence in the application for a person skilled in the art to understand the invention defined by the claims, having regard to the Examiner's rejections.

(1) Regarding the limitation that the effervescent couple is about 5% to about 80%: As the Examiner recognizes, the instant application teaches a range of between about 5% and about 95%, and preferably between 30% and about 80% (page 4, lines 20-24). Furthermore, the inventors also taught, and claim, about 20% to about 80%. (original claim 8, present claim 23). It is also observed that the examples of the application illustrate concentrations of the effervescent couple of 36% (Example 1) and about 72% (Example 2). Consequently, it appears that the claims have been rejected on the basis that there is no explicit recitation of the range as recited in claims 22 and 84, although the claimed range is within the scope of the express teaching of the application. This is very

similar to the facts of *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976), *appeal after remand*, 646 F.2d 527, 209 USPQ 554 (CCPA 1981). In *Wertheim* the applicant's invention was of a process for making freeze-dried instant coffee. The applicant sought the advantage of the filing date of a Swiss application which described a step of the process as achieving a solid concentration of "25 to 60% and gave specific examples of 36% and 50%." The claims in question specified a concentration of "between 35% and 60%." The court held that the Patent and Trademark Office failed to establish a *prima facie* case of noncompliance with the description requirement. The Office presented no evidence that one skilled in the art would not view the narrower range as within the applicant's invention or that "there is in fact any distinction in terms of the operability of [the] process or of the achieving of any described result between the claimed lower limit of solids content and that disclosed in the Swiss application." (Id., 541 F.2d at 264, 191 USPQ at 98). As the Court further explained, the determination is whether the invention sought to be protected by the inventors in the claims at issue "is part of the invention that [the inventors] described as *theirs* in the specification. That what appellants claim as patentable to them is less than what they describe as their invention is not conclusive if their specification also reasonably describes that which they do claim. (A)pplicants frequently discover during the course of prosecution that only a part of what they invented and originally claimed is patentable." (Id., 541 F.2d at 263, 191 USPQ at 97, *emphasis in the original.*)

Further to the Examiner's remark that "the instant application teaches a range of between about 5% and 95%, and preferably between 30% and about 80%," (*emphasis added*), the application recites the quoted ranges at the place identified,

and teaches a great deal more, including values having the recited ranges as well as other ranges within those quoted. Furthermore, the specific end-points of the claimed range are recited in the broad and preferred ranges quoted by the Examiner, as well as the concentration in Example 2 at greater than 78%, lending further support and credence to the choice of those specific values. It is respectfully suggested that Applicants have indeed conveyed to one skilled in the art that, at the time the application was filed, they had possession of the claimed invention, specifically regarding the amount of effervescent couple between about 5% and about 80%. It is respectfully requested that this aspect of the rejection be withdrawn.

(2) Turning next to the rejection regarding to the limitation that the couple is greater than the amount necessary for tablet disintegration: The Examiner states that "the specification doesn't contain any reference to what amount this may be or where this limitation may be found." This view is respectfully traversed.

In particular, the examples of the application provide specific direction to one skilled in the art as to the amounts that would be necessary for tablet disintegration. These values alone cover a range of 36 to greater than about 78%. Furthermore, the application teaches that there be sufficient effervescent material such that the "evolved gas is more than about 5cm³ but less than about 30cm³." (page 5, lines 5-7). Furthermore, the original and currently claimed concentration ranges provide additional direction for the amounts necessary for tablet disintegration. Consequently, Applicants have provided substantial teachings such that one skilled in the art, with limited experimentation, can ascertain the amount of

effervescent couple "greater than the amount necessary for tablet disintegration."

Additionally, it is observed that the limitation under consideration is not recited in the abstract, but rather in combination with the concentration limitation of "about 5% and about 80%." Consequently, the weight percent limitation provides a substantial teaching that is merely modified by the limitation that the amount be sufficient for tablet disintegration.

It is respectfully requested that this aspect of the rejection also be withdrawn.

At the time of the rejection, claims 22-24, 26-36 and 83-87 were further rejected under 35 U.S.C. §102(b) as being anticipated by *DiSanto* (U.S. 6,117,912, hereinafter *DiSanto*). Consequently, all then-pending claims except claim 25 directed to the further incorporation of a bioadhesive for increasing contact time between the tablet and oral mucosa, were rejected under §102(b). This rejection is respectfully traversed.

The Examiner relies on *DiSanto's* Example 3 that discloses a sublingual formulation of selegiline hydrochloride (an acid salt of selegiline and hydrochloric acid). The formulation of Example 3 contains 5 mg of the drug, 100 mg of citric acid, 185 mg of sodium bicarbonate and 10 mg of fumaric acid. The Examiner asserts that sodium bicarbonate in the formulation qualifies as the claimed "effervescent couple" on its own. Since sodium bicarbonate cannot be an effervescent couple, i.e., comprising two components, it appears, without there being an explicit statement in the Office Action, that the Examiner is suggesting that, even if citric acid were not present in the formulation, sodium bicarbonate would produce effervescence by reacting with the hydrochloric acid in the selegiline salt. For this reason, the Examiner uses only the

weight of sodium bicarbonate to determine the weight of the "effervescent couple" in Example 3. On this basis, the Examiner calculates that the amount of sodium bicarbonate in Example 3 is 61% by weight and concludes that *DiSanto* anticipates claim 22 (which recites from 5% to 80% of the "effervescent couple" by weight).

It is respectfully suggested that the Examiner misconstrues the term "effervescent couple." First of all, the instant claims recite a "couple," not just one "agent." Clearly, sodium bicarbonate cannot, by itself, be a "couple." Even if, as the Examiner argues, the "effervescent couple" could be produced *in situ* by hydrochloric acid in the drug and sodium bicarbonate, the citric acid, as well as the fumaric acid, present in the formulation cannot be ignored and must also be part of such "couple." If anything, since the HCl adds more acid, it accentuates the fact that *DiSanto* does not teach or suggest the range of claim 22.

Further, in addition to the numerical weight limitation, the instant claims also require that the amount of the effervescent couple be sufficient for tablet disintegration. If the Examiner's view is adopted that, e.g., the citric and fumaric acids can be ignored and the acid in selegiline is the source of acid for the effervescent couple, the example is inadequate to anticipate the instant claims.

The formulation in Example 3 of *DiSanto* contains 5 mg of selegiline hydrochloride. Accordingly, based on molecular weight calculations, the weight of hydrochloric acid in the selegiline salt and in the formulation is less than 1 mg. Even if the reaction between sodium bicarbonate and the trivial amount of hydrochloric acid in the selegiline salt does take place, the effervescent effect would be minimal. The amount of gas evolved from such a reaction would be very small, and thus

insufficient even for noticeable effervescence, let alone for tablet disintegration.

When the claims of the instant application are read on *DiSanto's* Example 3, the combination of citric acid (and, additionally, the fumaric acid also present) and sodium bicarbonate could qualify as an "effervescent couple." Considering the combined weight of citric acid and sodium bicarbonate, or both citric and fumaric acid plus sodium bicarbonate, the amount of effervescent couple in the Example 3 is substantially greater than 80% and thus outside the range of claim 22. The same argument is also true for all independent and dependent claims as currently presented for examination. Even assuming, *arguendo*, that sodium bicarbonate alone qualifies as an "effervescent couple," the amount of such "effervescent couple" in the formulation of Example 3 as discussed above, it would not be sufficient for tablet disintegration due to minimal gas evolution. Under any of these alternatives, *DiSanto* does not anticipate claim 22.

Furthermore, *DiSanto* does not anticipate claim 30. In its free form, selegiline is a tertiary amine: a base with a fairly high pK_a . As one skilled in the art would recognize, the dissociation equilibrium for an acid salt of selegiline may be illustrated by the equation: $B + H^+ \rightleftharpoons BH^+$, where B denotes free selegiline, H^+ is the proton of the salt-forming acid (e.g., hydrochloric acid), and BH^+ is the acid salt of selegiline (e.g., selegiline hydrochloride). In terms of claim 30, B is the *unionized* form of selegiline and BH^+ is its *ionized* form.

Reading claim 30 on *DiSanto's* Example 3, the only plausible candidates for the recited "pH adjusting substance" is either citric acid and/or fumaric acid, assuming that they are present in excess of the amount required for reaction with the amount of sodium bicarbonate. However, for a basic drug (such

as free selegiline), addition of an acid should not and does not change the pH to favor the *unionized* form of the drug. To the contrary, referring to the equation above, the addition of fumaric and/or citric acid (H^+) shifts the equilibrium toward the acid salt of selegiline (BH^+), which is the *ionized* form. Thus, the formulation of Example 3 does not contain a pH adjusting substance that could changes the pH of a local environment "to favor unionized form of the drug" as recited in the claim.

Finally, the Examiner asserts that Example 3 is anticipatory because slegiline HCl operates as both the active drug ingredient and as a pH-adjusting substance. This view is respectfully traversed.

To begin with, such a view misconstrues the instant claims because a reasonable reading of the claims requires a pH-adjusting substance in addition to the active ingredient. Furthermore, there is nothing in *DiSanto* to suggest that anything in the tablet formulation has been included for the purpose of adjusting the pH, in other words, for any purpose other than effervescence. If that is being read into the claims, it is only with the benefit of Applicants' teaching and such an analytical approach is not appropriate.

In summary, a closer examination of Example 3 of *DiSanto* shows that the formulation of the example, considering the acids and sodium bicarbonate in combination, contains greater than 98% of an effervescent couple, as that term is defined and claimed in the present invention. Consequently, it is significantly outside the range of the instant claims and cannot anticipate the claims. *DiSanto* also teaches nothing about the amount of effervescent materials other than the specific amounts in Example 3. Furthermore, it teaches nothing about the requirements of designing an effervescent system for driving drugs across the mucosal barrier. Neither does it

provide a teaching, suggestion or motivation as to how to modify the amount of effervescent material in any particular way. In those instances where the claims of the instant invention specifically include, e.g., a pH-adjusting substance or a non-effervescent penetration enhancer, *DiSanto* offers nothing. Properly interpreted, *DiSanto* is not an anticipatory reference, particularly not with regard to the instant claims. Withdrawal of the rejection under §102(b) is respectfully requested.

Claims 22 and 25 are rejected under 35 U.S.C. §103(a) as being unpatentable over *DiSanto*, further in view of *Tsuk et al.* (U.S. 3,972,995, hereinafter *Tsuk*). *Tsuk* is said to relate to dosage forms for buccal administration of a drug. In use, the dosage form is applied to the inside of the oral cavity, such that the drug is exposed to a small area of the oral mucosa while isolating the drug from the remainder of the oral cavity, thus rapidly achieving high drug blood levels (col. 1, lines 65 - col. 2, line 7 and col. 2, lines 40-48). This aspect of the rejection is respectfully traversed.

To begin with, independent claim 22 is not only not anticipated by *DiSanto*, it is also not obvious in view of the reference, either alone or further in view of *Tsuk*. *DiSanto* is deficient as a reference for all of the reasons explained above. The arguments presented make it clear that not only can it not anticipate claim 22, but it is so devoid of teachings with regard to the present invention that it is ineffective in view of the standards ordinarily applied with regard to a rejection on the basis of obviousness as well. For example, it teaches nothing about the amount of effervescent materials other than the specific amounts in Example 3. It also teaches nothing about the requirements of designing an effervescent system for driving drugs across the mucosal barrier. Neither does it

provide a teaching, suggestion or motivation as to how to modify the amount of effervescent material in any particular way.

To the extent that *Tsuk* is offered as a basis for rendering obvious claim 25, it too is ineffective. *Tsuk* discloses a construction that includes a water insoluble film and materials designed to accept an active drug. The construction is then adhered to the mucosa to allow the drug to become available. *Tsuk* does not relate to a tablet as required by the instant claims; it includes insoluble materials and a form that are contrary to the teaching of the present invention as a whole. There is no motivation in either of the references to combine them with one another, particularly since only a single example of *DiSanto* is relied on for the rejection.

It is respectfully suggested that the combination of *DiSanto* and *Tsuk* are ineffective to support a rejection under 35 U.S.C. §103(a) and that the rejection should be withdrawn.

As it is believed that all of the rejections set forth in the Official Action have been fully met, favorable reconsideration and allowance are earnestly solicited.

If, however, for any reason the Examiner does not believe that such action can be taken at this time, it is respectfully requested that he telephone Applicants' attorney at (908) 654-5000 in order to overcome any additional objections which he might have.

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If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

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Respectfully submitted,

By 

Harvey L. Cohen

Registration No.: 28,365

LERNER, DAVID, LITTENBERG,

KRUMHOLZ & MENTLIK, LLP

600 South Avenue West

Westfield, New Jersey 07090

(908) 654-5000

Attorneys for Applicant

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